

=> fil capl; d que 16

FILE 'CAPLUS' ENTERED AT 10:23:43 ON 20 FEB 2004

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FILE COVERS 1907 - 20 Feb 2004 VOL 140 ISS 8

FILE LAST UPDATED: 18 Feb 2004 (20040218/ED)

*inventor  
search*

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L1 281 SEA FILE=CAPLUS ABB=ON THIELE G?/AU  
L2 634 SEA FILE=CAPLUS ABB=ON MCDONALD T?/AU  
L3 234 SEA FILE=CAPLUS ABB=ON TUMA D?/AU  
L4 48 SEA FILE=CAPLUS ABB=ON KLASSEN L?/AU  
L5 131 SEA FILE=CAPLUS ABB=ON SORRELL M?/AU  
L6 5 SEA FILE=CAPLUS ABB=ON L1 AND L2 AND L3 AND L4 AND L5

=> d ibib ab 16 1-5

L6 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:797189 CAPLUS

DOCUMENT NUMBER: 130:192979

TITLE: Soluble proteins modified with acetaldehyde and malondialdehyde are immunogenic in the absence of adjuvant

AUTHOR(S): Thiele, Geoffrey M.; Tuma, Dean J.  
; Willis, Monte S.; Miller, Jacqueline A.;  
McDonald, Thomas L.; Sorrell, Michael  
F.; Klassen, Lynell W.

CORPORATE SOURCE: Departments of Internal Medicine, Pathology and Microbiology, University of Nebraska Medical Center, Omaha, NE, 68105, USA

SOURCE: Alcoholism: Clinical and Experimental Research (1998), 22(8), 1731-1739

CODEN: ACRSDM; ISSN: 0145-6008

PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Recent studies have shown that the alc. metabolites malondialdehyde and acetaldehyde can combine to form a stable adduct (MAA) on proteins. This adduct has been detected in the livers of rats chronically consuming ethanol, and serum antibodies to MAA have been obsd. at significantly higher concns. in ethanol-fed when compared with pair-fed or chow-fed control rats. More recently, preliminary studies have strongly suggested that the MAA adduct is capable of stimulating antibody responses to sol. proteins in the absence of adjuvants. The antibodies produced recognize

either the MAA epitope or the carrier protein itself. Therefore, it was the purpose of this study to examine the potential immunogenicity of MAA-modified exogenous proteins in the absence of adjuvants. Balb/c mice were immunized in the presence or absence of adjuvant with different concns. of unmodified or MAA-modified proteins. The antibody response to both the MAA epitope and unmodified protein epitopes were detd. by ELISA. In the absence of adjuvant, significant antibody responses were induced to both the MAA epitope and nonmodified protein epitopes. Smaller immunizing doses of MAA-protein conjugate favored the prodn. of antibodies to nonmodified proteins, whereas larger doses induced a strong anti-MAA response. In studies to begin detg. a mechanism for the specificity of the response in the absence of adjuvants, peritoneal macrophages were found to bind and degrade MAA-adducted proteins through the use of a scavenger receptor. This indicated that MAA-adducted proteins may be specifically taken up and epitopes presented to the humoral immune system in the absence of adjuvants. Importantly, these are the first data showing that an alc.-related metabolite can induce an antibody response in the absence of adjuvant and suggesting a mechanism by which antibody to the MAA adduct or its carrier (exogenous or endogenous) proteins may be generated in vivo.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:410650 CAPLUS

DOCUMENT NUMBER: 127:30338

TITLE: Novel acetaldehyde and malondialdehyde protein adducts as markers for alcohol liver disease

INVENTOR(S): Thiele, Geoffrey M.; McDonald, Thomas L.; Tuma, Dean J.; Klassen, Lynell W.; Sorrell, Michael F.

PATENT ASSIGNEE(S): Board of Regents of the University of Nebraska, USA; Thiele, Geoffrey M.; McDonald, Thomas L.; Tuma, Dean J.; Klassen, Lynell W.; Sorrell, Michael F.

SOURCE: PCT Int. Appl., 42 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9715599	A1	19970501	WO 1996-US17833	19961025
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9711173	A1	19970515	AU 1997-11173	19961025
US 5939535	A	19990817	US 1997-817018	19970408
PRIORITY APPLN. INFO.:		US 1995-5929P	P	19951027
		WO 1996-US17833	W	19961025

OTHER SOURCE(S): MARPAT 127:30338

AB A novel protein adduct is disclosed which is assocd. with the presence of alc. liver disease. The adduct is a hybrid product of malondialdehyde and acetaldehyde which act synergistically to bind hepatic proteins. The adduct is highly immunogenic and fluorescent. Methods of detection are also disclosed including monoclonal and polyclonal antibodies.

L6 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:385692 CAPLUS

DOCUMENT NUMBER: 127:4091

TITLE: High fluorescence specific immune enhancing factor and methods of use for same

INVENTOR(S): Thiele, Geoffrey M.; McDonald, Thomas

**L.; Tuma, Dean J.; Klassen, Lynell W.; Sorrell, Michael F.**  
PATENT ASSIGNEE(S): Board of Regents of the University of Nebraska, USA;  
Thiele, Geoffrey M.; McDonald, Thomas, L.; Tuma, Dean,  
J.; Klassen, Lynell W.; Sorrell, Michael F.  
SOURCE: PCT Int. Appl., 48 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9715324	A1	19970501	WO 1996-US17240	19961025
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9676654	A1	19970515	AU 1996-76654	19961025
AU 726344	B2	20001102		
EP 873136	A2	19981028	EP 1996-939501	19961025
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000505056	T2	20000425	JP 1997-516852	19961025
US 6120777	A	20000919	US 1997-849024	19970527
PRIORITY APPLN. INFO.:			US 1995-5959P	P 19951027
			WO 1996-US17240	W 19961025

AB A high fluorescence specific immune enhancing factor and methods of its use are described. The factor comprises a malondialdehyde-acetaldehyde adduct which can be detected in the picomolar range. The specific immunoenhancing factor allowing for a shorter time course for the prodn. of antibody and of higher titer antibodies without the need for adjuvant. The factor may further be used as a general fluorescent label for immunol. techniques and can be used to visualize protein interactions and to monitor protein purifn. procedures. Conjugate of malondialdehyde/acetaldehyde adduct (MAA) and rabbit plasma protein was prepd. as immunogen by treating the plasma protein with acetaldehyde in the presence of malondialdehyde. Polyclonal antibody against MAA-modified rabbit plasma protein was raised, purified and biotinylated for ELISA. MAA is a specific immunoenhancing factor and is useful for prepg. vaccine. MAA-modified protein (or antigen) raises not only antibody to MAA but also antibody to the specific protein (or antigen).

L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:529233 CAPLUS

DOCUMENT NUMBER: 121:129233

TITLE: Detection of reduced acetaldehyde protein adducts using a unique monoclonal antibody

AUTHOR(S): **Klassen, Lynell W.; Tuma, Dean J.; Sorrell, Michael F.; McDonald, Thomas L.; DeVasure, Jane M.; Thiele, Geoffrey M.**

CORPORATE SOURCE: Alcohol Res. Cent., Omaha Veterans Adm. Med. Cent., Omaha, NE, 68198-3332, USA

SOURCE: Alcoholism: Clinical and Experimental Research (1994), 18(1), 164-71  
CODEN: ACRSDM; ISSN: 0145-6008

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Acetaldehyde (AA), the major product of alc. metab., has been shown to bind to proteins in vivo and form chem. adducts. These AA-protein adducts have been shown to alter protein structure and function and may result in tissue damage. Recent reports have shown that polyclonal antibodies can be produced that recognize proteins modified in vitro with AA in the

presence of sodium cyanoborohydride (NaCNBH<sub>3</sub>), a strong reducing (R) agent. Antibodies prepd. in this way have been shown to recognize proteins in the livers of rats fed alc. chronically. Because multiple AA-protein adducts can be recognized by polyclonal antisera, and a variety of adducts may be formed in vitro or in vivo, this study was designed to develop monoclonal antibodies specific for proteins modified by AA. In addn., adducts formed under R conditions are probably chem. different than those formed under nonreducing (NR) conditions, and monoclonal antibodies may provide the specificity required to distinguish these chem. differences. Balb/c mice were immunized with bovine brain tubulin that was modified by treatment with 5 mM AA for 7 days under NR conditions. Sera from immunized animals were tested for antibody activity to the immunogen (protein-NR) and for cross-reactivity to protein-R and unmodified protein. Although the highest serum antibody titers were seen toward the NR adduct, antibodies to the R adduct were also detected. This activity difference was independent of the carrier protein, because NR and R bovine serum albumin, keyhole limpet hemocyanin, and actin also gave similar results when used as the adducted protein. Surprisingly, all the monoclonal antibodies (RT1.1, RT1.2, RT1.3, and RT1.4) produced by hybridomas generated from spleen cells from NR-tubulin immunized mice recognized the R and not the NR adduct. One of these hybridomas (RT1.1) produces an IgG2b antibody that reacts with all tested proteins that have been modified with AA under chem. R conditions. Because of its monoclonal specificity, this antibody may be useful in probing for the presence of R AA-protein adducts made both in vitro and in vivo.

L6 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1994:527657 CAPLUS

DOCUMENT NUMBER: 121:127657

TITLE: Specificity to N-ethyl lysine of a monoclonal antibody to acetaldehyde-modified proteins prepared under reducing conditions

AUTHOR(S): Thiele, Geoffrey M.; Wegter, Kirk M.;  
Sorrell, Michael F.; Tuma, Dean J.;  
McDonald, Thomas L.; Klassen, Lynell  
W.

CORPORATE SOURCE: Med. Cent., Univ. Nebraska, Omaha, NE, 68198, USA

SOURCE: Biochemical Pharmacology (1994), 48(1), 183-9

CODEN: BCPA6; ISSN: 0006-2952

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A monoclonal antibody has been developed that recognizes only protein-acetaldehyde (AA) adducts prepd. under reducing conditions: 5 mM AA with 30 mM sodium cyanoborohydride overnight at 37.degree.. This monoclonal antibody is a mouse IgG2b that has been designated RT1.1. The primary adduct formed when proteins are exposed to acetaldehyde under reducing conditions is N-Et lysine (NEL). To examine the epitope specificity of RT1.1, inhibition ELISAs were developed using NEL and other possible inhibitors, such as arginine, ethylamine, lysine and proteins modified with AA under non-reducing conditions. RT1.1 (at half-max. optical d., 50 ng/mL) was inhibited only by NEL and was independent of the carrier or the pH of the buffer used in the ELISA. Further evidence indicating that NEL is the epitope recognized by RT1.1 was obtained using mouse and human epidermal growth factor (EGF). Both proteins contain one alpha amino group but only the human-EGF contains lysine residues with epsilon amino groups. In expts. where these two proteins were modified with AA under reducing conditions, RT1.1 reacted only with human-EGF. These studies demonstrate that RT1.1 is specific for NEL that is formed by the ethylation of proteins with acetaldehyde under reducing conditions. Addnl., these studies demonstrate that the procedures and methods used herein may be useful for characterizing other antibodies prepd. to AA-modified proteins under a variety of defined in vitro chem. conditions.

=> d his 17-

(FILE 'CAPLUS' ENTERED AT 10:21:12 ON 20 FEB 2004)  
L7 1 S ALCOHOL/TI AND L6  
SEL RN

FILE 'REGISTRY' ENTERED AT 10:22:59 ON 20 FEB 2004  
L8 5 S E1-E5

FILE 'CAPLUS' ENTERED AT 10:23:43 ON 20 FEB 2004

=> fil reg; d scan 18

FILE 'REGISTRY' ENTERED AT 10:24:19 ON 20 FEB 2004  
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STRUCTURE FILE UPDATES: 18 FEB 2004 HIGHEST RN 651705-73-6  
DICTIONARY FILE UPDATES: 18 FEB 2004 HIGHEST RN 651705-73-6

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

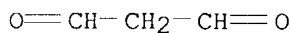
Please note that search-term pricing does apply when  
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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more  
information enter HELP PROP at an arrow prompt in the file or refer  
to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

*structures  
from  
inventors'  
work*

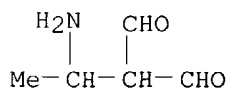
L8 5 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN  
IN Propanedial (9CI)  
MF C3 H4 O2  
CI COM



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

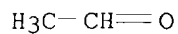
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):5

L8 5 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN  
IN Propanedial, (1-aminoethyl)- (9CI)  
MF C5 H9 N O2



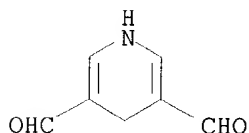
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L8 5 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN  
IN Acetaldehyde (8CI, 9CI)  
MF C2 H4 O  
CI COM



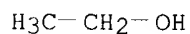
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L8 5 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN  
IN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro- (9CI)  
MF C7 H7 N O2



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

L8 5 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN  
IN Ethanol (9CI)  
MF C2 H6 O  
CI COM



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

ALL ANSWERS HAVE BEEN SCANNED

=> fil reg; d stat que l11  
FILE 'REGISTRY' ENTERED AT 10:35:03 ON 20 FEB 2004  
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STRUCTURE FILE UPDATES: 18 FEB 2004 HIGHEST RN 651705-73-6  
DICTIONARY FILE UPDATES: 18 FEB 2004 HIGHEST RN 651705-73-6

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

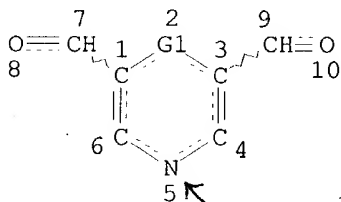
Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more  
information enter HELP PROP at an arrow prompt in the file or refer  
to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

L9

STR



CH-Ak  
@14 15

CH-CH2-Ph  
@11 12 13

VAR G1=CH2/14/11  
NODE ATTRIBUTES:  
CONNECT IS E1 RC AT 15  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE  
L11 112 SEA FILE=REGISTRY SSS FUL L9

100.0% PROCESSED 105742 ITERATIONS  
SEARCH TIME: 00.00.02

112 ANSWERS

=> fil capl; d que nos 118;d que nos 120; s 118 or 120

FILE 'CAPLUS' ENTERED AT 10:35:04 ON 20 FEB 2004  
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FILE COVERS 1907 - 20 Feb 2004 VOL 140 ISS 8  
FILE LAST UPDATED: 18 Feb 2004 (20040218/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L9	STR
L11	112 SEA FILE=REGISTRY SSS FUL L9
L12	49 SEA FILE=CAPLUS ABB=ON L11
L13	373513 SEA FILE=CAPLUS ABB=ON LIVER/OBI
L14	12336 SEA FILE=CAPLUS ABB=ON CIRRHOSIS/OBI
L15	211686 SEA FILE=CAPLUS ABB=ON ALCOHOLISM/OBI
L17	6 SEA FILE=CAPLUS ABB=ON L12 AND (L13 OR L14 OR L15)
L18	2 SEA FILE=CAPLUS ABB=ON L17 AND P/DT

*patents (not date limited)*

L9	STR
L11	112 SEA FILE=REGISTRY SSS FUL L9
L12	49 SEA FILE=CAPLUS ABB=ON L11
L13	373513 SEA FILE=CAPLUS ABB=ON LIVER/OBI
L14	12336 SEA FILE=CAPLUS ABB=ON CIRRHOSIS/OBI
L15	211686 SEA FILE=CAPLUS ABB=ON ALCOHOLISM/OBI
L17	6 SEA FILE=CAPLUS ABB=ON L12 AND (L13 OR L14 OR L15)
L18	2 SEA FILE=CAPLUS ABB=ON L17 AND P/DT
L19	4 SEA FILE=CAPLUS ABB=ON L17 NOT L18
L20	4 SEA FILE=CAPLUS ABB=ON L19 NOT PY>1998

*-non-patent references limited by date*

L29 6 L18 OR L20

=> fil uspatf; d que nos 122

FILE 'USPATFULL' ENTERED AT 10:35:05 ON 20 FEB 2004  
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 19 Feb 2004 (20040219/PD)  
FILE LAST UPDATED: 19 Feb 2004 (20040219/ED)  
HIGHEST GRANTED PATENT NUMBER: US6694518  
HIGHEST APPLICATION PUBLICATION NUMBER: US2004034897  
CA INDEXING IS CURRENT THROUGH 19 Feb 2004 (20040219/UPCA)  
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 19 Feb 2004 (20040219/PD)  
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2003



## USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2003

>>> USPAT2 is now available. USPATFULL contains full text of the <<<  
>>> original, i.e., the earliest published granted patents or <<<  
>>> applications. USPAT2 contains full text of the latest US <<<  
>>> publications, starting in 2001, for the inventions covered in <<<  
>>> USPATFULL. A USPATFULL record contains not only the original <<<  
>>> published document but also a list of any subsequent <<<  
>>> publications. The publication number, patent kind code, and <<<  
>>> publication date for all the US publications for an invention <<<  
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<  
>>> records and may be searched in standard search fields, e.g., /PN, <<<  
>>> /PK, etc. <<<

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>>> enter this cluster. <<<  
>>> <<<  
>>> Use USPATALL when searching terms such as patent assignees, <<<  
>>> classifications, or claims, that may potentially change from <<<  
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

L9 STR  
L11 112 SEA FILE=REGISTRY SSS FUL L9  
L22 2 SEA FILE=USPATFULL ABB=ON L11

=> fil toxcenter; d que nos 126

FILE 'TOXCENTER' ENTERED AT 10:35:05 ON 20 FEB 2004  
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FILE COVERS 1907 TO 17 Feb 2004 (20040217/ED)

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TOXCENTER has been enhanced with new files segments and search fields.  
See HELP CONTENT for more information.

TOXCENTER thesauri in the /CN, /CT, and /MN fields incorporate the  
MeSH 2004 vocabulary. See <http://www.nlm.nih.gov/mesh/> and  
[http://www.nih.gov/pubs/yechebull/nd03/nd03\\_mesh.html](http://www.nih.gov/pubs/yechebull/nd03/nd03_mesh.html) for a description  
on changes.

L9 STR  
L11 112 SEA FILE=REGISTRY SSS FUL L9  
L23 10 SEA FILE=TOXCENTER ABB=ON L11  
L24 6 SEA FILE=TOXCENTER ABB=ON L23 NOT PY>1998  
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HEPATIC?  
L26 1 SEA FILE=TOXCENTER ABB=ON L24 AND L25

=> dup rem 129,122,126

FILE 'CAPLUS' ENTERED AT 10:35:19 ON 20 FEB 2004  
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FILE 'TOXCENTER' ENTERED AT 10:35:19 ON 20 FEB 2004  
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PROCESSING COMPLETED FOR L29  
PROCESSING COMPLETED FOR L22  
PROCESSING COMPLETED FOR L26  
L30 8 DUP REM L29 L22 L26 (1 DUPLICATE REMOVED)  
ANSWERS '1-6' FROM FILE CAPLUS  
ANSWERS '7-8' FROM FILE USPATFULL

=> d ibib abs hitstr 1-8; fil hom

L30 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1  
ACCESSION NUMBER: 1997:410650 CAPLUS  
DOCUMENT NUMBER: 127:30338  
TITLE: Novel acetaldehyde and malondialdehyde protein adducts  
as markers for alcohol **liver** disease  
INVENTOR(S): Thiele, Geoffrey M.; McDonald, Thomas L.; Tuma, Dean  
J.; Klassen, Lynell W.; Sorrell, Michael F.  
PATENT ASSIGNEE(S): Board of Regents of the University of Nebraska, USA;  
Thiele, Geoffrey M.; McDonald, Thomas L.; Tuma, Dean  
J.; Klassen, Lynell W.; Sorrell, Michael F.  
SOURCE: PCT Int. Appl., 42 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: **Patent**  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9715599	A1	19970501	WO 1996-US17833	19961025
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9711173	A1	19970515	AU 1997-11173	19961025
US 5939535	A	19990817	US 1997-817018	19970408
PRIORITY APPLN. INFO.:			US 1995-5929P	P 19951027
			WO 1996-US17833	W 19961025

OTHER SOURCE(S): MARPAT 127:30338

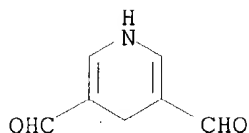
AB A novel protein adduct is disclosed which is assocd. with the presence of alc. liver disease. The adduct is a hybrid product of malondialdehyde and acetaldehyde which act synergistically to bind hepatic proteins. The adduct is highly immunogenic and fluorescent. Methods of detection are also disclosed including monoclonal and polyclonal antibodies.

IT **61354-90-3**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(alkyl or benzyl derivs. and protein adducts; novel acetaldehyde and malondialdehyde protein adducts as markers for **alc. liver** disease)

RN 61354-90-3 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro- (9CI) (CA INDEX NAME)



L30 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN  
ACCESSION NUMBER: 2002:157534 CAPLUS  
DOCUMENT NUMBER: 136:189119  
TITLE: Lipofuscins for inducing and intensifying the tanning mechanisms of the skin and usage in cosmetic or dermatological preparations  
INVENTOR(S): Blatt, Thomas; Berens, Werner; Staeb, Franz; Wolber, Rainer  
PATENT ASSIGNEE(S): Beiersdorf A.-G., Germany  
SOURCE: PCT Int. Appl., 31 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002015861	A1	20020228	WO 2001-EP9655	20010821
W: US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
DE 10041272	A1	20020307	DE 2000-10041272	20000823
EP 1311233	A1	20030521	EP 2001-971943	20010821
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				

PRIORITY APPLN. INFO.: DE 2000-10041272 A 20000823  
WO 2001-EP9655 W 20010821

AB The invention relates to the use of one or several substances selected from the group contg. lipofuscins for tanning the skin, and to cosmetic or dermatol. prepn. which contain lipofuscins. Lipofuscins enhance the synthesis of melanin and protect the skin from oxidative stress. Thus lipofuscin was prep. by homogenizing liver tissue and isolating mitochondria in repeated washing and centrifugation steps; the final pellet from a sucrose gradient was exposed to UV irradiation for 20 h. Lipid peroxidation takes place during UV exposure and malondialdehyde is formed that reacts with Schiff's bases from free amino groups of proteins to form lipofuscins. A W/O cream contained (wt./wt.%): paraffin oil 10.00; petrolatum 4.00; wool wax alc. 1.00; PEG-7-hydrated castor oil 3.00; aluminum stearate 0.40; glycerin 2.00; preservatives, dyes, perfume q.s.; lipofuscin 0.20; water to 100.00.

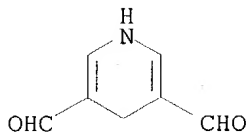
IT 61354-90-3, 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-  
61354-90-3D, 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-,  
N,N'-derivs.

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(lipofuscins for inducing and intensifying tanning mechanisms of skin and usage in cosmetic or dermatol. prepn.)

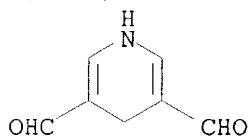
RN 61354-90-3 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro- (9CI) (CA INDEX NAME)



RN 61354-90-3 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:259037 CAPLUS

DOCUMENT NUMBER: 129:26068

TITLE: Blue fluorescence generated during lipid oxidation of rat **liver** microsomes cannot be derived from malonaldehyde but can be from other aldehyde species

AUTHOR(S): Inoue, Tadamichi; Kikugawa, Kiyomi

CORPORATE SOURCE: School of Pharmacy, Tokyo University of Pharmacy and Life Science (Formerly Tokyo College of Pharmacy), Tokyo, 192-0392, Japan

SOURCE: Biological & Pharmaceutical Bulletin (1998), 21(4), 319-325

CODEN: BPBLEO; ISSN: 0918-6158

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Generation of blue fluorescence together with phospholipid hydroperoxides and aldehyde species in rat liver microsomes during oxidn. with FeCl<sub>2</sub>-ADP-ascorbic acid was monitored, and the kind of lipid oxidn. products participating in the formation of blue fluorescence was investigated. Contents of phospholipid hydroperoxides increased in the early stages of oxidn., and decreased in the more advanced stages of oxidn. Contents of components that liberated malonaldehyde, 4-hydroxyalkenals and other unsatd. aldehydes under the acidic assay conditions were increased in the advanced stage of oxidn. Water-sol. blue fluorescence with a max. at 440-450 nm detd. after sepn. through gel filtration accumulated in the advanced stage of oxidn., and was characterized as resistant to borohydride treatment and to be little dependent on pH values of the solvent. Wavelength of the max. fluorescence and characteristics of the fluorescence were similar to those of fluorescence with maxima at 440-450 nm formed by reaction of unoxidized microsomes, bovine serum albumin or methylamine with alkenals, and different from those of fluorescence with maxima at above 460 nm obtained by the reaction with a mixt. contg. malonaldehyde. Hence, blue fluorescence accumulated in oxidized microsomes cannot be derived from free malonaldehyde but can be from other aldehyde species including alkenals.

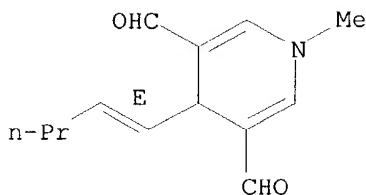
IT 208119-83-9P 208119-84-0P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(origin of the blue fluorescent species formed in lipid epoxidn. in **liver** microsomes)

RN 208119-83-9 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-1-methyl-4-(1E)-1-pentenyl-  
(9CI) (CA INDEX NAME)

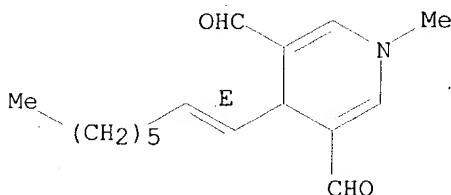
Double bond geometry as shown.



RN 208119-84-0 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-1-methyl-4-(1E)-1-octenyl- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:603204 CAPLUS

DOCUMENT NUMBER: 127:217337

TITLE: Epitope Characterization of Malondialdehyde-  
Acetaldehyde Adducts Using an Enzyme-Linked  
Immunosorbent Assay

AUTHOR(S): Xu, Dongsheng; Thiele, Geoffrey M.; Kearley, Mark L.;  
Haugen, Mark D.; Klassen, Lynell W.; Sorrell, Michael  
F.; Tuma, Dean J.

CORPORATE SOURCE: Department of Veterans Affairs Alcohol Research Center  
and Departments of Internal Medicine Biochemistry  
Molecular Biology and Pathology Microbiology,  
University of Nebraska Medical Center, Omaha, NE,  
68105, USA

SOURCE: Chemical Research in Toxicology (1997), 10(9), 978-986  
CODEN: CRTOEC; ISSN: 0893-228X

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Malondialdehyde (MDA) and acetaldehyde react together with proteins in a synergistic manner and form hybrid protein adducts, designated as MAA adducts. In a previous study, a polyclonal antibody specific for MAA-protein adducts was used in an immunoassay to detect the presence of MAA adducts in livers of ethanol-fed rats. In the present study, the specific epitope recognized by the antibody was defined and the chem. of MAA adduct formation was further characterized. When several synthetic analogs were tested for their ability to inhibit antibody binding in a competitive ELISA, the results indicated that the major determinant of antibody binding was a highly fluorescent cyclic adduct composed of two mols. of MDA and one of acetaldehyde. The structure of this adduct was

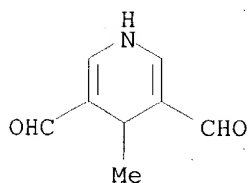
shown to be a 4-methyl-1,4-dihydropyridine-3,5-dicarbaldehyde deriv. of an amino group of a protein. Examn. of MAA adduct formation with a variety of proteins indicated that in addn. to this specific fluorescent adduct, MAA adducts were also comprised of other non-fluorescent products. The amt. of fluorescent epitopes present on a given protein was the major determinant of antibody binding as assessed in a competitive ELISA, although the efficiency of inhibition of antibody binding by these fluorescent epitopes on MAA-adducted proteins varied depending upon the particular protein. However, when these MAA-adducted proteins were hydrolyzed with Pronase, the concn. of these modified proteins necessary to achieve 50% inhibition of antibody binding in a competitive ELISA fell into a much narrower range of values, indicating that protein hydrolysis equalized the accessibility of the antibody to bind the epitope on these various derivatized proteins. In summary, a cyclic fluorescent adduct of defined structure has been identified as the epitope recognized by our MAA adduct antibody. In addn. to this specific adduct, MAA adducts are also comprised of other non-fluorescent products.

IT 71970-43-9P 78524-77-3P 80840-97-7P  
194999-57-0P 194999-58-1P 194999-59-2P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(epitope characterization of malondialdehyde-acetaldehyde adducts using ELISA)

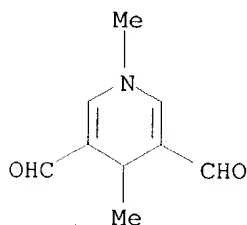
RN 71970-43-9 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-4-methyl- (9CI) (CA INDEX NAME)



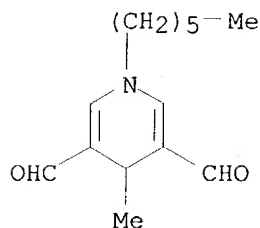
RN 78524-77-3 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-1,4-dimethyl- (9CI) (CA INDEX NAME)

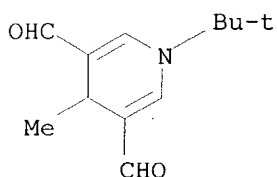


RN 80840-97-7 CAPLUS

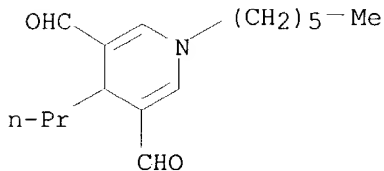
CN 3,5-Pyridinedicarboxaldehyde, 1-hexyl-1,4-dihydro-4-methyl- (9CI) (CA INDEX NAME)



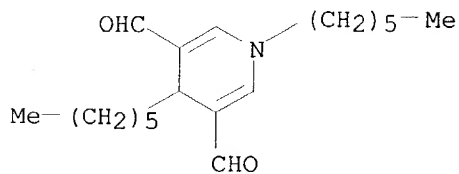
RN 194999-57-0 CAPLUS  
 CN 3,5-Pyridinedicarboxaldehyde, 1-(1,1-dimethylethyl)-1,4-dihydro-4-methyl- (9CI) (CA INDEX NAME)



RN 194999-58-1 CAPLUS  
 CN 3,5-Pyridinedicarboxaldehyde, 1-hexyl-1,4-dihydro-4-propyl- (9CI) (CA INDEX NAME)



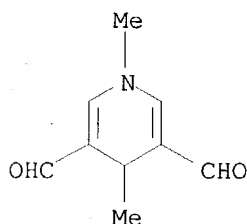
RN 194999-59-2 CAPLUS  
 CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihexyl-1,4-dihydro- (9CI) (CA INDEX NAME)



L30 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN  
 ACCESSION NUMBER: 1989:53979 CAPLUS  
 DOCUMENT NUMBER: 110:53979  
 TITLE: Determination of malonaldehyde in oxidized lipids by the Hantzsch fluorometric method  
 AUTHOR(S): Kikugawa, Kiyomi; Kato, Tetsuta; Iwata, Atsushi  
 CORPORATE SOURCE: Tokyo Coll. Pharm., Hachioji, 192-03, Japan  
 SOURCE: Analytical Biochemistry (1988), 174(2), 512-21  
 CODEN: ANBCA2; ISSN: 0003-2697  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB A sensitive and reliable Hantzsch fluorometric method was developed for

detn. of malonaldehyde in oxidized lipids. The principle of the method is based on the formation of highly fluorescent 1,4-dimethyl-1,4-dihydropyridine-3,5-dicarbaldehyde MI by reaction of malonaldehyde, methylamine, and acetaldehyde under neutral conditions. Compd. MI formed could be estd. by HPLC. Free malonaldehyde, that liberated under neutral conditions (labile forms), and that liberated by acid pretreatment (acid labile forms) could be detd. by use of the calibration curves of MI vs. malonaldehyde Na salt. Oxidized Me linoleate with a peroxide value of 1600 neg/mg contained 0.95 (free and labile) and 1.3 nmol (acid labile) malonaldehyde/mg, oxidized sardine oil with a peroxide values of 640 neg/mg contained 1.1 (free and labile) and 3.0 nmol (acid labile) malonaldehyde/mg, and the lipid fraction of oxidized rat liver microsomes contained <0.2 (free and labile) and 0.8 nmol (acid labile) malonaldehyde/mg. The malonaldehyde contents were much lower than those obtained by traditional 2-thiobarbituric acid test. Apparently, the malonaldehyde contents, both free and labile, and acid labile forms, in oxidized lipids are too low to be taken into account.

IT 78524-77-3; 1,4-Dimethyl-1,4-dihydropyridine-3,5-dicarbaldehyde  
RL: FORM (Formation, nonpreparative)  
(formation of, in malonaldehyde detn. in oxidized lipids by Hantzsch fluorometric method)  
RN 78524-77-3 CAPLUS  
CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-1,4-dimethyl- (9CI) (CA INDEX NAME)



L30 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1986:18235 CAPLUS

DOCUMENT NUMBER: 104:18235

TITLE: Degradation of fluorescent substances derived from malondialdehyde and amino compounds in rat liver microsomes

AUTHOR(S): Yoden, Kazuaki; Matsuzaki, Reiko; Iio, Toshihiro; Tabata, Toshikazu

CORPORATE SOURCE: Showa Coll. Pharm. Sci., Tokyo, 154, Japan

SOURCE: Yakugaku Zasshi (1985), 105(9), 855-61

CODEN: YKKZAJ; ISSN: 0031-6903

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

AB The degrdn. of fluorescent substances, N-substituted-1,4-dihydropyridine-3,5-dialdehyde derivs., derived from the reaction of malondialdehyde (MDA), which is one of the end-degradative products during lipid peroxidn., with various amino compds., was studied in rat liver microsomal fractions as a model for accumulation and metab. of lipofuscins. The MDA initially forms a conjugated Schiff base with the amines at >1 mol. MDA/amine, and this Schiff base forms the dihydropyridine deriv. The fluorescent substances from the reaction of MDA with 1-aminopentane, 1-aminoheptane, 1-aminodecane, and phenylethylamine (PEA) rapidly changed into water-sol. compds. On the other hand, the fluorescent compds. from short-length amino compds. such as methylamine had a little or no change. The degrdn. system required NADP and was inhibited by CO. Furthermore, in microsomal fractions from phenobarbital-pretreated rats, the rate of



degrdn. increased. The degradative compds. of the fluorescent substance from MDA with [14C]phenylethylamine were sepd. by HPLc. Two major water-sol. fluorescent compds., 4-methyl-1,4-dihydropyridine-3,5-dialdehyde and 1-phenylethyl-4-hydroxy-4-methyl-1,4-dihydropyridine-3,5-dialdehyde, and minor fat-sol. fluorescent compds. were isolated. All of these isolated degradative compds. retained 1,4-dihydropyridine structure, and exhibited also the same max. excitation and emission spectra at 392 and 448 nm, resp., as those of the native fluorescent substance. The microsomal degrdn. of fluorescent substances related to MDA (apparently involving cytochrome P 450) evidently was dependent on the structure of the N-alkyl side-chain of the amino compds.

IT 78524-77-3 84269-60-3 99506-68-0

99506-69-1 99506-70-4 99506-71-5

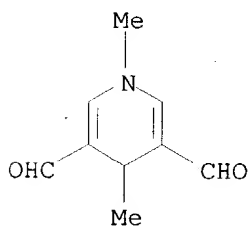
99506-72-6 99506-73-7 99506-75-9

RL: PRP (Properties)

(degrdn. of, by **liver** microsomes)

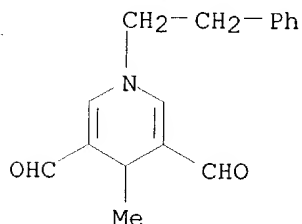
RN 78524-77-3 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-1,4-dimethyl- (9CI) (CA INDEX NAME)



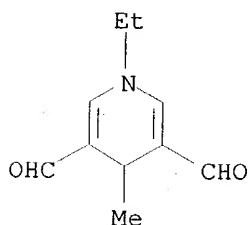
RN 84269-60-3 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-4-methyl-1-(2-phenylethyl)- (9CI) (CA INDEX NAME)



RN 99506-68-0 CAPLUS

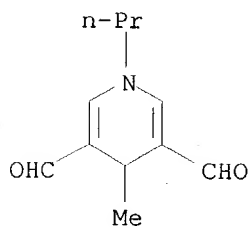
CN 3,5-Pyridinedicarboxaldehyde, 1-ethyl-1,4-dihydro-4-methyl- (9CI) (CA INDEX NAME)



RN 99506-69-1 CAPLUS

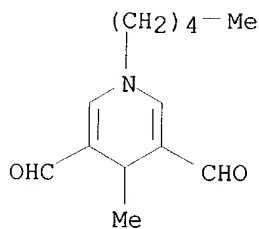
CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-4-methyl-1-propyl- (9CI) (CA

INDEX NAME)



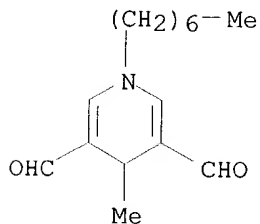
RN 99506-70-4 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-4-methyl-1-pentyl- (9CI) (CA INDEX NAME)



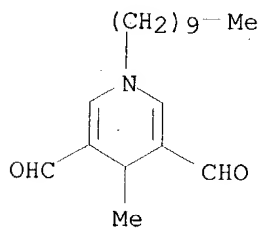
RN 99506-71-5 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1-heptyl-1,4-dihydro-4-methyl- (9CI) (CA INDEX NAME)



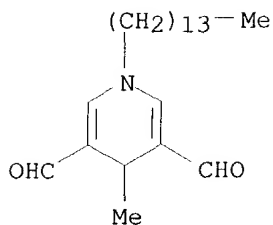
RN 99506-72-6 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1-decyl-1,4-dihydro-4-methyl- (9CI) (CA INDEX NAME)



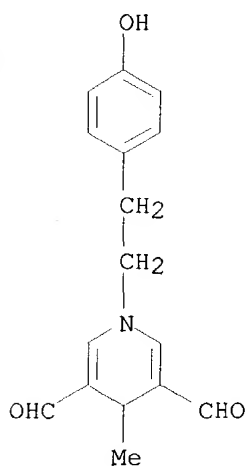
RN 99506-73-7 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-4-methyl-1-tetradecyl- (9CI) (CA INDEX NAME)



RN 99506-75-9 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-1-[2-(4-hydroxyphenyl)ethyl]-4-methyl- (9CI) (CA INDEX NAME)



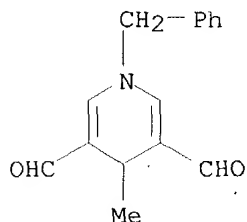
IT 99506-74-8

RL: PRP (Properties)

(degrdn. of, by **liver** microsomes, products and mechanism of)

RN 99506-74-8 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-4-methyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



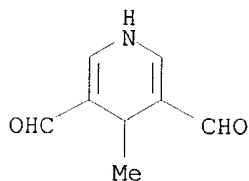
IT 71970-43-9 99491-47-1

RL: FORM (Formation, nonpreparative)

(formation of, from malondialdehyde-phenylethylamine reaction product by **liver** microsomes, cytochrome P 450 in)

RN 71970-43-9 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-4-methyl- (9CI) (CA INDEX NAME)

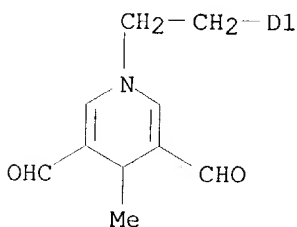


RN 99491-47-1 CAPLUS

CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-1-[2-(hydroxyphenyl)ethyl]-4-methyl- (9CI) (CA INDEX NAME)



D1-OH



L30 ANSWER 7 OF 8 USPATFULL on STN

ACCESSION NUMBER: 2000:124557 USPATFULL

TITLE: High fluorescence specific immune enhancing factor and methods of use for same

INVENTOR(S): Thiele, Geoffrey M., Omaha, NE, United States

McDonald, Thomas L., Omaha, NE, United States

Tuma, Dean J., Omaha, NE, United States

Klassen, Lynell W., Omaha, NE, United States

Sorrell, Michael F., Omaha, NE, United States

PATENT ASSIGNEE(S): The Board of Regents of the University of Nebraska, Lincoln, NE, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6120777		20000919
	WO 9715324		19970501
APPLICATION INFO.:	US 1997-849024		19970527 (8)
	WO 1996-US17240		19961025
			19970527 PCT 371 date
			19970527 PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	US 1995-5959P	19951027 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	MacMillan, Keith D.	

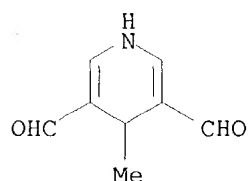
ASSISTANT EXAMINER: Ponnaluri, P.  
LEGAL REPRESENTATIVE: Zarley, McKee, Thomte, Voorhees & Sease  
NUMBER OF CLAIMS: 16  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 16 Drawing Figure(s); 9 Drawing Page(s)  
LINE COUNT: 1302

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a malondialdehyde-acetaldehyde adduct which acts as a specific immune-enhancing factor. In addition to its highly specific and immunogenic properties, the factor is highly fluorescent. It has an excitation frequency of about 398 nanometers and an absorbance of about 460 nanometers. The factor is also highly reactive and is also adducted to antigens including complex proteins, lipids, carbohydrates or DNA.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 71970-43-9DP, conjugates  
(malondialdehyde/acetaldehyde adduct is used as high fluorescence specific immune enhancing factor)  
RN 71970-43-9 USPATFULL  
CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro-4-methyl- (9CI) (CA INDEX NAME)



L30 ANSWER 8 OF 8 USPATFULL on STN

ACCESSION NUMBER: 1999:96486 USPATFULL  
TITLE: Acetaldehyde and malondialdehyde protein adducts  
INVENTOR(S): Thiele, Geoffrey M., Omaha, NE, United States  
McDonald, Thomas L., Omaha, NE, United States  
Tuma, Dean J., Omaha, NE, United States  
Klassen, Lynell W., Omaha, NE, United States  
Sorrell, Michael F., Omaha, NE, United States  
PATENT ASSIGNEE(S): The Board of Regents of the University of Nebraska,  
Lincoln, NE, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5939535		19990817
APPLICATION INFO.:	US 1997-817018		19970408 (8)
	WO 1996-US17833		19961025
			19970408 PCT 371 date
			19970408 PCT 102(e) date

	NUMBER	DATE
PRIORITY INFORMATION:	US 1995-5929P	19951027 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Hutzell, Paula K.	
ASSISTANT EXAMINER:	Ungar, Susan	
LEGAL REPRESENTATIVE:	Zarley, McKee, Thomte, Voorhees & Seas	
NUMBER OF CLAIMS:	4	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	16 Drawing Figure(s); 9 Drawing Page(s)	

LINE COUNT: 1152

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A novel protein adduct is disclosed which is associated with the presence of alcohol liver disease. The adduct is a hybrid product of malondialdehyde and acetaldehyde which act synergistically to bind hepatic proteins. The adduct is highly immunogenic and fluorescent. Methods of detection are also disclosed including monoclonal and polyclonal antibodies.

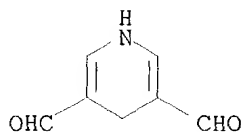
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 61354-90-3

(alkyl or benzyl derivs. and protein adducts; novel acetaldehyde and malondialdehyde protein adducts as markers for alc. liver disease)

RN 61354-90-3 USPATFULL

CN 3,5-Pyridinedicarboxaldehyde, 1,4-dihydro- (9CI) (CA INDEX NAME)



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